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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/674,172	01/04/2000	Andreas Bohle	10890-2MIS:J	3048

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EXAMINER
ZEMAN, ROBERT

ART UNIT	PAPER NUMBER
1645	9

DATE MAILED: 12/10/2001

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/674,172	BOHLE ET AL.	
	Examiner	Art Unit	
	Robert A Zeman	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE ____ MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *19 September 2001* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,8-16 and 20-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,8-16 and 20-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *8* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The amendment and response filed on 9-16-2001 is acknowledged. Claims 1, 3, 8, 11-13, 15-16, 20 and 22 have been amended. Claims 5-7, 17-19 and 24-25 have been canceled. Claims 1-4, 8-16 and 20-23 are pending and currently under examination.

Claim Objections Withdrawn

The objection to claim 3 for containing an obvious grammatical error is withdrawn in light of the amendment thereto.

Claims Rejections Withdrawn

The rejection of claims 1 and 16 under 35 U.S.C. 112, second paragraph, as being rendered vague and indefinite by the use of the term "region of infection" is withdrawn in light of the amendment thereto.

The rejection of claim 1 under 35 U.S.C. 112, second paragraph, as being rendered vague and indefinite by the use of the term "effective" is withdrawn in light of the amendment thereto.

The rejection of claims 5 and 17 under 35 U.S.C. 112, second paragraph, as being rendered vague and indefinite by the use of the term "tuberculosis complex" is withdrawn. Cancellation of said claims has rendered the rejection moot.

The rejection of claims 15 and 22 under 35 U.S.C. 112, second paragraph, as being rendered vague and indefinite by the use of the term "1 to about 10 wt.%" is withdrawn in light of the amendment thereto.

The rejection of claim 24 under 35 U.S.C. 112, second paragraph, for the use of the phrase "particularly" is withdrawn. Cancellation of said claim has rendered the rejection moot.

The rejection of claim 25 under 35 U.S.C. 112, second paragraph, for the use of the phrase "such as" is withdrawn. Cancellation of said claim has rendered the rejection moot.

The rejection of claims 24-25 under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process is withdrawn. Cancellation of said claims has rendered the rejection moot.

The rejection of claims 5-6 and 24-25 under 35 U.S.C. 102(b) as being anticipated by Herr et al. is withdrawn. Cancellation of said claims has rendered the rejection moot.

The rejection of claims 5-7, 17-19 and 24-25 under 35 U.S.C. 103(a) as being unpatentable over Herr et al. (Journal of Urology Vol. 141, pages 22-29, 1989) in view of Morton (GB2179858A) is withdrawn. Cancellation of said claims has rendered the rejection moot.

Claim Rejections Maintained

35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The rejection of claims 1-4, 8-12, 16 and 23 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the use of **Bacillus Calmette-Guerin (BCG)** for the therapeutic treatment of condylomata acuminata, does not reasonably provide enablement for the use of **all** *Mycobacterium* species/strains for the therapeutic treatment of **all** disease conditions caused by papilloma virus infections is maintained for the reasons outlined in the

rejection of claims 1-6, 8-12, 16-18 and 23-25 in the previous Office action. Applicant has amended the claims to read only on the use of BCG in the treatment of disease conditions caused by papilloma virus infection. However, this amendment is insufficient to overcome the rejection since the specification does not provide enablement for the use of any *Mycobacterium* strains/species for the treatment of **all** disease conditions caused by papilloma virus infections. The specification provides ample factual evidence that BCG can be used to treat condylomata acuminata, which is associated with papilloma virus infection. Applicant has failed give direction on what disease conditions, other than condylomata acuminata, would meet the limitations of the claims and has provided no evidence that any benefit to the treated subject would be obtained from treatment with BCG. Human papilloma virus is associated with a myriad of human "disease conditions" including: verruca plantaris, verruca vulgaris, verruca plana, epidermodysplasia verruciformis (benign and squamous cell carcinoma), condyloma acuminatum, laryngeal papilloma, Butcher's warts, focal epithelial hyperplasia, cervical intraepithelial neoplasia, cervical carcinoma, oral papilloma, flat warts, macular lesions, Bowen's disease, bladder carcinomas and bladder papillomas. Applicant has not taught how to use BCG to treat any of the aforementioned disease conditions. Given the lack of success in the art, the lack of working examples, and the unpredictability of the generation of a therapeutic response in a living organism, the specification, as filed, is not enabling for the use of BCG as a therapeutic treatment for any and all disease conditions caused by papilloma virus infections.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The rejection of claims 1-4 and 8-15 under 35 U.S.C. 112, second paragraph, as being vague and indefinite as they are lacking in positive active steps of the methods is maintained for reasons outlined in the rejection of claims 1-15 in the previous Office action. Applicant has failed to address this rejection in his response to the previous Office action.

The rejection of claim 8 under 35 U.S.C. 112, second paragraph, as being rendered vague and indefinite by the confusing language used in reciting the multiple ranges that encompass the limitations of the claim is maintained for reasons of record. Applicant argues that said claim language is clear is scope. The aforementioned claim language is confusing making it impossible to determine the metes and bounds of the claimed invention should be rewritten so that there is a clear demarcation of each limitation.

35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The rejection of claims 1, 2 and 9 under 35 U.S.C. 102(b) as being anticipated by Herr et al. is maintained for reasons of record.

Applicant argues:

1. Herr et al. is not concerned with the treatment of a papilloma virus disease condition but rather describes the treatment of superficial bladder tumors with topical instillation of BCG.

2. No cream is used.

3. Human papilloma virus is not associated with bladder carcinoma or bladder papillomas.

4. According to Westenend et al. (IDS-8) papilloma is used to describe grade 1 papillary tumor when referring to superficial bladder tumors.

5. According to Westenend et al. there is no association between papillary urothelial carcinoma (papillomas) and HPV-associated condyloma (warts).

Applicant's arguments have been fully considered and deemed to be non-persuasive.

As outlined in the previous Office action, the instant invention is drawn to methods of treating disease conditions (warts papillomas, carcinomas etc.) caused by the papilloma virus. Said method comprises the application of a composition comprising a *Mycobacterium* (bacillus Calmette-Guerin). The recited methods of use also recite the use of said composition use as a topical cream whose use is preceded by ablative surgery of the region of infection (i.e. removal of papilloma etc.).

Herr et al. disclose a method of treating superficial bladder carcinomas and papillomas caused by human papilloma virus (HPV) with bacillus Calmette-Guerin (BCG). Herr et al. also disclose that the BCG treatment can follow the resection of the tumor (see materials and methods section beginning on page 22). Said disclosure anticipates all the limitations of the rejected claims.

The Westenend et al. reference deals with only 7 of the 70+ serotypes of HPV and cannot be used to buttress the argument that HPV has no association with bladder tumors or papillomas. As stated by Westenend et al. (see introduction on page 198) "HPV has been implicated in the pathogenesis of several human cancers". Additionally, Westenend et al. deal only with the possible role of "high risk HPV and not all the different serotypes. Additionally, Applicant is reminded that claims 1 and 9 are drawn to all papilloma viruses not just HPV.

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., composition is a cream) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The rejection of claims 1-4, 8-16 and 20-23 under 35 U.S.C. 103(a) as being unpatentable over Herr et al. (Journal of Urology Vol. 141, pages 22-29, 1989) in view of Morton (GB2179858A) is maintained for reasons of record.

Applicant argues:

1. Herr et al. is not concerned with the treatment of a papilloma virus disease condition but rather describes the treatment of superficial bladder tumors with topical instillation of BCG.

2. No cream is used.

3. Human papilloma virus is not associated with bladder carcinoma or bladder papillomas.

4. According to Westenend et al. (IDS-8) papilloma is used to describe grade 1 papillary tumor when referring to superficial bladder tumors.

5. According to Westenend et al. there is no association between papillary urothelial carcinoma (papillomas) and HPV-associated condyloma (warts).

6. There is no motivation to modify the composition described by Morten et al.

As outlined in the previous Office action, the instant invention is drawn to a composition for treating disease conditions (warts etc.) caused by the papilloma virus and methods of using a composition comprising a *Mycobacterium* (bacillus Calmette-Guerin) and a keratolytic agent (salicylic acid). The recited methods of use of said composition include its use as a topical cream whose use is preceded by ablative surgery (laser) of the region of infection (i.e. removal of papilloma etc.).

Herr et al. disclose a method of treating superficial bladder carcinomas and papillomas caused by human papilloma virus (HPV) with bacillus Calmette-Guerin (BCG). Herr et al. also disclose that the BCG treatment can follow the resection of the tumor (see materials and methods section beginning on page 22). Herr et al. differs from the instant invention in that it does not disclose the use of BCG to treat condylomata acuminata (genital warts) nor does it explicitly

disclose the use of a laser to ablate the wart before the onset of treatment (said use is a common surgical practices and hence is obvious) or the use of salicylic acid as keratolytic agent in the treatment composition. Morton discloses the use of salicylic acid as a keratolytic agent in a topical compound that can be used to treat viral skin diseases including condylomata acuminata (see page 2 lines 15-17). Morton further discloses that the salicylic acid may comprise "up to 15% by weight" of the composition (see page 1, line 32). Finally, Morton discloses multiple composition forms for the topical application of the composition including a concentrated solution, a gel and an ointment. Since the use of creams/gels/ointments is commonly used to deliver a therapeutic composition to a treatment site it would have been obvious to one of skill of the art to use the BCG, as disclosed by Herr et al., in a salicylic acid-containing topical cream/gel/ointment as disclosed by Morton in order to take advantage of the benefits of using a topical cream/gel (i.e. therapeutic composition adheres to area to be treated). One would expect the resulting composition to be an effective treatment for condylomata acuminata (warts) since BCG has been demonstrated to be an effective treatment for papillomas, as disclosed by Herr et al.), which also has human papilloma virus as a causative agent.

The Westenend et al. reference deals with only 7 of the 70+ serotypes of HPV and cannot be used to buttress the argument that HPV has no association with bladder tumors or papillomas. As stated by Westenend et al. (see introduction on page 198) "HPV has been implicated in the pathogenesis of several human cancers". Additionally, Westenend et al. deal only with the possible role of "high risk HPV and not all the different serotypes. Additionally, Applicant is reminded that claims 1 and 9 are drawn to all papilloma viruses not just HPV.

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., composition is a cream) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

With regard to Applicants assertion there would be no motivation to modify the composition disclosed by Morton: the BCG containing composition of Herr et al. is being modified to take advantage of the benefits of using a topical cream/gel (disclosed by Morton).

New Grounds of Rejection

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 11-13 and 16 are rendered vague and indefinite by the use of the term "area of infection". It is unclear what Applicant is referring to. Is the "area of infection" the site of papilloma virus infection or some other infection facilitated by the papilloma virus infection? As written, it is impossible to determine the metes and bounds of the claimed invention.

Claim 1 is rendered vague and indefinite by the use of the term "treatment dose" It is unclear to what constitutes a "treatment dose". What criteria are used to ascertain whether a given dose is a "treatment dose"? As written, it is impossible to determine the metes and bounds of the claimed invention.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert A Zeman whose telephone number is (703) 308-7991. The examiner can normally be reached on M-Th 7:30 am - 5:00 pm and Alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful Donna Wortman, Primary Examiner, can be reached on (703) 308-1032. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

DONNA WORTMANN
PRIMARY EXAMINER

Robert A. Zeman
November 19, 2001